Auditory hallucinations: Does a continuum of severity entail continuity in mechanism?

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Word count: 1,156

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The continuum view holds that psychotic symptoms vary along dimensions such as distress, vividness and duration in clinical and non-clinical groups. At one extreme, symptoms are so severe and disabling that they require treatment and sometimes hospitalisation. At the other end of the spectrum, individuals display similar symptoms without significant distress, disability or dysfunction.

Recently, the continuum model has come under pressure from different directions[1]. Its postulation of gradual quantitative transitions across a continuum of symptom expression lends itself well to empirical evaluation. In support of the model, research efforts have identified similarities in psychosis-like experiences between healthy and psychiatric groups, from which common underlying mechanisms are sometimes inferred. This search for commonality might follow from an assumption that different levels of explanation map neatly onto each other. While similarities between groups in features of symptom expression might align with commonalities at the neurobiological level, they equally may not. Complex systems lend themselves to analysis at multiple levels of organisation, and we should be wary of inferring from a continuum at one level that there must also be a continuum at another.

A case in point is the example of auditory hallucinations. There are few discernible differences in the descriptive features of experience between psychotic and non-psychotic hallucinations[2]. Some non-clinical voice-hearers report vivid and frequent hallucinations, third-person hallucinations, and personification, as well as some negative contents, resembling the hallucinations of people diagnosed with a psychotic disorder. In the absence of differential phenomenological markers, a common approach in making diagnostic and treatment decisions is to focus on the presence of distress, or impairments in social, occupational or other important areas of functioning, as a threshold for clinically significant symptoms[3]. An over-emphasis on distress and functioning, however, may obscure important continuities and discontinuities across different population groups.

One example includes evidence of categorical differences within people presenting with psychosis-like experiences in the general population. At least two different continua have been proposed: a continuum of symptom expression, distributed across clinical and non-clinical groups, and a (dis)continuum of risk whereby only a subset of individuals are vulnerable to developing psychosis[4,5]. Even with a continuum of symptom expression, it seems likely that important discontinuities will exist. Studies are now investigating distinct non-clinical subgroups such as professional psychics, voice-hearers

with no psychiatric diagnosis, people at high risk or in the prodrome phase of psychosis, as well as individuals who score highly on measures of psychosis proneness. The extent to which these form a heterogeneous group within the category of non-clinical hallucinations is still unclear, and future research will be helpful in determining whether such groups differ on variables relating to aetiology, phenomenology, subjective appraisals, and underlying mechanisms.

Neurobiological studies also reveal a complex pattern of continuity and discontinuity between pathological and nonpathological experiences. First, results of imaging studies show that brain changes in people with medical conditions who have hallucinations (acquired deafness, narcolepsy, etc.) are localised and specific[6,7], which contrasts with the widespread changes observed in hallucinating individuals with schizophrenia[8]. Second, studies of neurobiological processes involving direct comparisons of clinical and non-clinical samples show similarities as well as important differences. A functional Magnetic Resonance Imaging (fMRI) study comparing a healthy and psychiatric group with frequent hallucinations revealed continuity in activation of the superior temporal gyrus and bilateral inferior frontal gyri[9], while a structural MRI study showed comparable changes in the insular region[10].

Other evidence involving direct group comparisons points to discontinuity in mechanisms. Garrison et al (this issue[11]) examined the structure of the paracingulate sulcus (PCS), a region in the anterior medial prefrontal cortex implicated in reality monitoring. Structural MRI scans revealed shorter PCS length in the psychotic group with frequent hallucinations, which differentiated them from the non-psychiatric comparison groups (with and without hallucinations).

A limitation of all three studies (each conducted with the same large non-clinical sample from the Netherlands) is the absence of a psychosis comparison group without hallucinations, without which specificity to hallucinations and the contribution of other symptom mechanisms cannot be assessed. Nonetheless, the finding of typical PCS lengths in the non-clinical group with hallucinations is in line with a recent cognitive study which failed to find reality-monitoring deficits in non-clinical individuals scoring high on measures of hallucination proneness[12]. In further support for discontinuity in process, the cognitive literature in non-clinical samples with hallucinations shows largely mixed results[5,12], although traditional difficulties in publishing negative findings likely act to bias the literature.

Further evidence of discontinuity in mechanisms includes pharmacological evidence that striatal dopaminergic overactivity may be specific to symptoms in psychosis. Positron Emission Tomography (PET) imaging studies suggest that elevated striatal dopamine production (which characterizes

psychosis) is not a feature of non-clinical groups with hallucinations[13]. Another interpretation of this finding is that hallucinations should not be considered a core feature of psychosis (or at least not as central a feature as striatal dopamine dysregulation), since they occur in both psychotic and non-psychotic groups, as well as other psychiatric and medical conditions with distinct underlying mechanisms. In support, classical texts refer to hallucinations as secondary (non-integral) feature of schizophrenia[14]. In any case, since antipsychotic medication seems only to benefit patients with increased striatal dopamine[15], a clinical implication of this finding is a caution about the introduction of antipsychotic medication until alternative medical causes for distressing hallucinations have been excluded.

An emerging theme from this recent literature is that there may be a mix of continuity and discontinuity in hallucination-related processes across the spectrum from wellness to disorder. One candidate for a continuous process is alteration in spontaneous auditory cortex activation, which may feature in both clinical and non-clinical hallucinations[11]. By contrast, candidates for discontinuous mechanisms include prefrontal reality-monitoring processes and striatal dopaminergic dysregulation, which appear more specific to hallucinations in psychosis. These points of difference might explain intact reality-monitoring and preserved insight in the non-clinical groups.

Further research into the neural and psychological processes underlying non-clinical hallucinations will likely clarify this picture. Methodologically robust designs should include appropriate psychiatric and non-psychiatric comparison groups, and a greater focus on potential differences between groups in medication, lifestyle and clinical risk factors. Greater attention should also be paid to co-occurring experiences (e.g., delusional thinking, negative symptoms) which are often neglected in non-clinical groups.

In conclusion, there are dangers in inferring continuity in mechanism from continuity in phenomenology, including a risk of incorrect treatment. On the other hand, discontinuity of mechanism between clinical and non-clinical groups presents opportunities for research. These include the development of sensitive measures to chart heterogeneity across the clinical divide and enhance the detection of individuals at risk of psychosis. Another challenge is to understand the therapeutic needs of people with different hallucination subtypes so that individuals can access support depending on symptom-specific needs. In the meantime, a graded approach to intervention (holding in mind the possibility of phenomenological continuity) is desirable, as is recognition of possible discontinuity in underlying mechanisms, with interventions tailored accordingly[16].

Acknowledgement: CF is supported by Wellcome Trust grant WT108720.

References

1. David A. Why we need more debate on whether psychotic symptoms lie on a continuum with normality. *Psychological medicine.* 2010;40(12):1935-1942.
2. Waters F, Fernyhough C. Hallucinations: a systematic review of points of similarity and difference across diagnostic classes. *Schizophrenia bulletin.* 2017;43(1):32-43.
3. Association AP. *Diagnostic and statistical manual of mental disorders (DSM-5®).* American Psychiatric Pub; 2013.
4. Claridge G. Single indicator of risk for schizophrenia: probable fact or likely myth? *Schizophrenia Bulletin.* 1994;20(1):151-168.
5. Johns LC, Kompus K, Connell M, et al. Auditory verbal hallucinations in persons with and without a need for care. *Schizophrenia bulletin.* 2014;40(Suppl_4):S255-S264.
6. Griffiths TD. Musical hallucinosis in acquired deafness: phenomenology and brain substrate. *Brain.* 2000;123(10):2065-2076.
7. Kaufmann C, Schuld A, Pollmächer T, Auer DP. Reduced cortical gray matter in narcolepsy: preliminary findings with voxel-based morphometry. *Neurology.* 2002;58(12):1852-1855.
8. Allen P, Modinos G, Hubl D, et al. Neuroimaging auditory hallucinations in schizophrenia: from neuroanatomy to neurochemistry and beyond. *Schizophrenia bulletin.* 2012;38(4):695-703.
9. Diederen KM, Daalman K, de Weijer AD, et al. Auditory hallucinations elicit similar brain activation in psychotic and nonpsychotic individuals. *Schizophrenia bulletin.* 2011;38(5):1074-1082.
10. van Lutterveld R, van den Heuvel MP, Diederen KM, et al. Cortical thickness in individuals with non-clinical and clinical psychotic symptoms. *Brain.* 2014;137(10):2664-2669.
11. Garrison JR, Fernyhough C, McCarthy-Jones S, Simons JS, Sommer IE. Paracingulate sulcus morphology and hallucinations in clinical and non-clinical groups. *Schizophrenia Bulletin.* 2019;In press.
12. Garrison JR, Moseley P, Alderson-Day B, Smailes D, Fernyhough C, Simons JS. Testing continuum models of psychosis: No reduction in source monitoring ability in healthy individuals prone to auditory hallucinations. *cortex.* 2017;91:197-207.
13. Howes OD, Shotbolt P, Bloomfield M, et al. Dopaminergic function in the psychosis spectrum: an [18F]-DOPA imaging study in healthy individuals with auditory hallucinations. *Schizophrenia bulletin.* 2012;39(4):807-814.
14. Bleuler E. *Dementia praecox or the group of schizophrenias (translated by J. Zinkin and N.D.C. Lewis).* New York: International University Press; 1911/1950.
15. Ćurčić-Blake B, Ford JM, Hubl D, et al. Interaction of language, auditory and memory brain networks in auditory verbal hallucinations. *Progress in neurobiology.* 2017;148:1-20.
16. Smailes D, Alderson-Day B, Fernyhough C, McCarthy-Jones S, Dodgson G. Tailoring cognitive behavioral therapy to subtypes of voice-hearing. *Frontiers in psychology.* 2015;6:1933.